

PART B—ISSUE FEE TRANSMITTAL

Complete and mail this form, together with applicable fees, to:

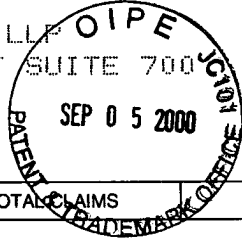
Box ISSUE FEE
Assistant Commissioner for Patents
Washington, D.C. 20231

MAILING INSTRUCTIONS: This form should be used for transmitting the ISSUE FEE. Blocks 1 through 4 should be completed where appropriate. All further correspondence including the Issue Fee Receipt, the Patent, advance orders and notification of maintenance fees will be mailed to the current correspondence address as indicated unless corrected below or directed otherwise in Block 1, by (a) specifying a new correspondence address; and/or (b) indicating a separate "FEE ADDRESS" for maintenance fee notifications.

CURRENT CORRESPONDENCE ADDRESS (Note: Legibly mark-up with any corrections or use Block 1)

KAREN B KING
MICHAEL BEST & FRIEDRICH LLP
ONE SOUTH PINCKNEY STREET SUITE 700
P O BOX 1806
MADISON WI 53701-1806

HM22/0605



Note: The certificate of mailing below can only be used for domestic mailings of the Issue Fee Transmittal. This certificate cannot be used for any other accompanying papers. Each additional paper, such as an assignment or formal drawing, must have its own certificate of mailing.

Certificate of Mailing

I hereby certify that this Issue Fee Transmittal is being deposited with the United States Postal Service with sufficient postage for first class mail in an envelope addressed to the Box Issue Fee address above on the date indicated below.

(Depositor's name)

(Signature)

(Date)

| APPLICATION NO. | FILING DATE | TOTAL CLAIMS | EXAMINER AND GROUP ART UNIT | DATE MAILED |
|-----------------------|---|--------------|-----------------------------|---------------|
| 09/475,958 | 12/30/99 | 028 | SISSON, B | 1655 06/05/00 |
| First Named Applicant | BITNER, 35 USC 154(b) term ext. = 0 Days. | | | |

TITLE OF INVENTION CELL CONCENTRATION AND LYSATE CLEARANCE USING PARAMAGNETIC PARTICLES

| ATTY'S DOCKET NO. | CLASS-SUBCLASS | BATCH NO. | APPLN. TYPE | SMALL ENTITY | FEE DUE | DATE DUE |
|-------------------|----------------|-------------|-------------|--------------|-----------|----------|
| 1 | 16026-9038 | 435-270.000 | N31 UTILITY | NO | \$1210.00 | 09/05/00 |

1. Change of correspondence address or indication of "Fee Address" (37 CFR 1.363). Use of PTO form(s) and Customer Number are recommended, but not required.

- ☐ Change of correspondence address (or Change of Correspondence Address form PTO/SB/122) attached.
- ☐ "Fee Address" indication (or "Fee Address" Indication form PTO/SB/47) attached.

2. For printing on the patent front page, list (1) the names of up to 3 registered patent attorneys or agents OR, alternatively, (2) the name of a single firm (having as a member a registered attorney or agent) and the names of up to 2 registered patent attorneys or agents. If no name is listed, no name will be printed.

- 1 Michael Best & Friedrich LLP
- 2 Grady J. Frenchick
- 3 Karen B. King

3. ASSIGNEE NAME AND RESIDENCE DATA TO BE PRINTED ON THE PATENT (print or type)
PLEASE NOTE: Unless an assignee is identified below, no assignee data will appear on the patent. Inclusion of assignee data is only appropriate when an assignment has been previously submitted to the PTO or is being submitted under separate cover. Completion of this form is NOT a substitute for filing an assignment.

(A) NAME OF ASSIGNEE PROMEGA CORPORATION

(B) RESIDENCE: (CITY & STATE OR COUNTRY) MADISON, WISCONSIN

Please check the appropriate assignee category indicated below (will not be printed on the patent)

- ☐ individual ☒ corporation or other private group entity ☐ government

4a. The following fees are enclosed (make check payable to Commissioner of Patents and Trademarks):

- ☒ Issue Fee
- ☒ Advance Order - # of Copies 10 @ \$3.00

4b. The following fees or deficiency in these fees should be charged to:

DEPOSIT ACCOUNT NUMBER 50-0842
(ENCLOSE AN EXTRA COPY OF THIS FORM)

- ☐ Issue Fee
- ☐ Advance Order - # of Copies _____

The COMMISSIONER OF PATENTS AND TRADEMARKS IS requested to apply the Issue Fee to the application identified above.

(Authorized Signature)

(Date)

Karen King

9/1/00

NOTE: The Issue Fee will not be accepted from anyone other than the applicant; a registered attorney or agent; or the assignee or other party in interest as shown by the records of the Patent and Trademark Office.

Burden Hour Statement: This form is estimated to take 0.2 hours to complete. Time will vary depending on the needs of the individual case. Any comments on the amount of time required to complete this form should be sent to the Chief Information Officer, Patent and Trademark Office, Washington, D.C. 20231. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND FEES AND THIS FORM TO: Box Issue Fee, Assistant Commissioner for Patents, Washington D.C. 20231

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TRANSMIT THIS FORM WITH FEE



UNITED STATES DEPARTMENT OF COMMERCE
Patent and Trademark Office

NOTICE OF ALLOWANCE AND ISSUE FEE DUE

HM227/005

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| APPLICATION NO. | FILING DATE | TOTAL CLAIMS | EXAMINER AND GROUP ART UNIT | DATE MAILED |
|-----------------------|-------------|--------------|-----------------------------|---------------|
| 09/475,958 | 12/30/99 | 028 | MISSION, B | 1-55 06/05/01 |
| First Named Applicant | BITNER, | | 35 USC 154(b) term ext. = | 0 Days. |

TITLE OF INVENTION CELL CONCENTRATION AND LYSATE CLEARANCE USING PARAMAGNETIC PARTICLES

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|-------------------|----------------|-----------|-------------|--------------|-----------|----------|
| 1 16026-9038 | 435-270.000 | N31 | UTILITY | NO | \$1210.00 | 02/05/01 |

THE APPLICATION IDENTIFIED ABOVE HAS BEEN EXAMINED AND IS ALLOWED FOR ISSUANCE AS A PATENT. PROSECUTION ON THE MERITS IS CLOSED.

THE ISSUE FEE MUST BE PAID WITHIN THREE MONTHS FROM THE MAILING DATE OF THIS NOTICE OR THIS APPLICATION SHALL BE REGARDED AS ABANDONED. THIS STATUTORY PERIOD CANNOT BE EXTENDED.

HOW TO RESPOND TO THIS NOTICE:

- I. Review the SMALL ENTITY status shown above.
If the SMALL ENTITY is shown as YES, verify your current SMALL ENTITY status:
 - A. If the status is changed, pay twice the amount of the FEE DUE shown above and notify the Patent and Trademark Office of the change in status, or
 - B. If the status is the same, pay the FEE DUE shown above.
- If the SMALL ENTITY is shown as NO:
 - A. Pay FEE DUE shown above, or
 - B. File verified statement of Small Entity Status before, or with, payment of 1/2 the FEE DUE shown above.
- II. Part B-Issue Fee Transmittal should be completed and returned to the Patent and Trademark Office (PTO) with your ISSUE FEE. Even if the ISSUE FEE has already been paid by charge to deposit account, Part B Issue Fee Transmittal should be completed and returned. If you are charging the ISSUE FEE to your deposit account, section "4b" of Part B-Issue Fee Transmittal should be completed and an extra copy of the form should be submitted.
- III. All communications regarding this application must give application number and batch number.
Please direct all communications prior to issuance to Box ISSUE FEE unless advised to the contrary.

IMPORTANT REMINDER: Utility patents issuing on applications filed on or after Dec. 12, 1980 may require payment of maintenance fees. It is patentee's responsibility to ensure timely payment of maintenance fees when due.

PATENT AND TRADEMARK OFFICE COPY

Notice of Allowability

Application No.

09/475,958

Examiner

Bradley L. Sisson

Applicant(s)

BITNER ET AL.

Art Unit

1655

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance and Issue Fee Due or other appropriate communication will be mailed in due course.

1. ☒ This communication is responsive to interview of 25 May 2000.
2. ☒ The allowed claim(s) is/are 1-25 and 27-29
3. ☒ The drawings filed on 30 December 1999 are acceptable.
4. ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).
 - a) ☐ All b) ☐ Some* c) ☐ None of the CERTIFIED copies of the priority documents have been
 1. ☐ received.
 2. ☐ received in Application No. (Series Code / Serial Number). _____
 3. ☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).
- * Certified copies not received: _____
5. ☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. & 119(e).

A SHORTENED STATUTORY PERIOD FOR REPLY to comply with the requirements noted below is set to EXPIRE **THREE MONTHS** FROM THE "DATE MAILED" of this Office Action. Failure to timely comply will result in ABANDONMENT of this application. Extensions of time may be available under the provisions of 37 CFR 1.136(a).

6. ☒ Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient. A SUBSTITUTE OATH OR DECLARATION IS REQUIRED.
7. ☐ Applicant MUST submit NEW FORMAL DRAWINGS
 - (a) ☐ because the originally filed drawings were declared by applicant to be informal.
 - (b) ☐ including changes required by the Notice of Draftsperson's Patent Drawing Review(PTO-948) attached
 - 1) ☐ hereto or 2) ☐ to Paper No. _____
 - (c) ☐ including changes required by the proposed drawing correction filed _____, which has been approved by the examiner.
 - (d) ☐ including changes required by the attached Examiner's Amendment / Comment.

Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the reverse side of the drawings. The drawings should be filed as a separate paper with a transmittal letter addressed to the Official Draftsperson.

8. ☐ Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Any reply to this letter should include, in the upper right hand corner, the APPLICATION NUMBER (SERIES CODE / SERIAL NUMBER). If applicant has received a Notice of Allowance and Issue Fee Due, the ISSUE BATCH NUMBER and DATE of the NOTICE OF ALLOWANCE should also be included.

Attachment(s)

- | | |
|--|---|
| 1 <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 2 <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3 <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 4 <input type="checkbox"/> Interview Summary (PTO-413), Paper No. _____ |
| 5 <input type="checkbox"/> Information Disclosure Statements (PTO-1449), Paper No. _____ | 6 <input checked="" type="checkbox"/> Examiner's Amendment/Comment |
| 7 <input type="checkbox"/> Examiner's Comment Regarding Requirement for Deposit of Biological Material | 8 <input checked="" type="checkbox"/> Examiner's Statement of Reasons for Allowance |
| | 9 <input type="checkbox"/> Other |

EXAMINER'S AMENDMENT

Oath/Declaration

1. The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

The oath or declaration is defective because:

Non-initialed and/or non-dated alterations have been made to the oath or declaration. See 37 CFR 1.52(c).

2. An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee.

Authorization for this examiner's amendment was given in a telephone interview with Grady J. Frenchick, Reg. No. 29,018, and Karen B. King, Reg. No. 41,898, on 25 May 2000.

The application has been amended as follows:

Claim 1. (Amended) A method of using magnetic particles to concentrate or harvest cells, comprising the steps of:

(a) combining [a solutions with] cells [contained therein] with magnetic particles under conditions wherein the cells form a complex with the magnetic particles, wherein said magnetic particles are selected from the group consisting of (1) pH dependent ion exchange particle and

Art Unit: 1655

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cont

(2) silica magnetic particle^s consisting essentially of a magnetic core coated with a siliceous oxide having a hydrous siliceous oxide adsorptive surface; and

(b) isolating the complex from the solution by application of magnetic force.

Claim 8. (Amended) A method of clearing a solution of disrupted biological material, according to steps comprising:

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378

(a) providing a solution comprising a disrupted biological material and a target nucleic acid;

B28

(b) combining the solution with second magnetic particles under conditions wherein the disrupted biological material selectively forms a complex with the second magnetic particles, wherein said second magnetic particles are selected from the group consisting of (1) pH dependent ion exchange particle^s and (2) silica magnetic particle^s consisting essentially of a magnetic core coated with a siliceous oxide having a hydrous siliceous oxide adsorptive surface; and

(c) separating the complex from the solution by application of magnetic force.

Claim 21. (Amended) A method of isolating a target nucleic acid from a disrupted biological material, comprising the target nucleic acid, a first non-target material, and a second non-target material, comprising the steps of:

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(a) combining a solution of the disrupted biological material with first magnetic particles under conditions wherein the first non-target material selectively forms a first complex with the first magnetic particles, wherein said first magnetic particles are selected from the group

Art Unit: 1655

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consisting of (1) pH dependent ion exchange particle^s and (2) silica magnetic particle^s consisting essentially of a magnetic core coated with a siliceous oxide having a hydrous siliceous oxide adsorptive surface;

(b) separating the first complex from the solution of disrupted biological material by application of magnetic force, forming a cleared solution comprising the target nucleic acid and the second non-target material;

(c) combining the cleared solution with second magnetic particles under conditions wherein the target nucleic acid adsorbs to the second magnetic particles, forming a second complex;

(d) isolating the second complex from the cleared solution;

(e) washing the second complex by combining the second complex with a wash solution and separating the second complex from the wash solution by magnetic force; and

(f) combining the washed second complex with an elution solution, under conditions wherein the target material is desorbed from the second magnetic particles.

Cancel claims 26 and 30-34.

3. The following is an examiner's statement of reasons for allowance: Claims 1-25 and 27-29 are allowable over the combined teachings of Dorn (US Patent 4,927,750), Van Vlasselaer et al., (US Patent 5,789,148), Nakahata (US Patent 5,861,315), the closest prior art of record.

4. Dorn, column 15, discloses use of colloidal silica particles that have been treated with gamma-glycidioxypropyltrimethoxysilane. Unlike the claimed method, the method of Dorn

Art Unit: 1655

teaches rendering the treated silica particles non-ionic by having the silica particles be passed through carbon and cation exchange resin. The colloidal particles do not bind to the cells but rather, are used in forming a portion of a continuing gradient such that mononuclear cells can be separated from other cells in the sample.

5. Van Vlasselaer et al., like that of Dorn, disclose density gradient centrifugation where colloidal silica particles are used; see columns 13-17.

6. Nakahata, column 5, discloses the use of magnetic beads for the selective separation of mononuclear cells from blood. Unlike the claimed method, Nakahata has antibodies conjugated to the surface of the magnetic particle.; see page 8. Unlike the claimed method, the magnetic particles are used to bind nucleic acid sequences, not bind other material found in the disrupted biological sample.

7. Accordingly, the prior art of record does not teach nor reasonably suggest the claimed method of either harvesting/concentrating cells or purifying nucleic acid wherein said methods cells or their remnants (disrupted biological material), are bound to magnetic particles s defined in claims 1, 8, and 21.

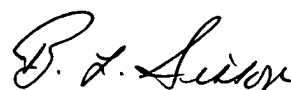
8. Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance."

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bradley L. Sisson whose telephone number is (703) 308-3978. The examiner can normally be reached on 6:30 a.m. to 5 p.m., Monday through Thursday.

Art Unit: 1655

10. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W Gary Jones can be reached on (703) 308-1152. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 305-3592 for regular communications and (703) 308-0294 for After Final communications.

11. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.



Bradley L. Sisson
Primary Examiner
Art Unit 1655

BLS
May 29, 2000